EXHIBIT B

Docket No.: ALZA-0141R (ARC02366) MAIL STOP "*EX PARTE* REEXAM"
Control No.: 90/007,772
Office Action Dated: June 20, 2006

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors: George V. Guittard, Francisco Jao, Susan M. Marks, David J. Kidney, Fernando E. Gumucio, Suneel Gupta, and Gayatri Sathyan
Patent No.: 6,919,092 B2
Issued: July 19, 2005
For: METHOD FOR THE MANAGEMENT OF INCONTINENCE

Confirmation No.: 3781
Examiner: Evelyn Huang
Technology Center Art Unit: 3991
Control No.: 90/007,772
Patentee: ALZA Corporation

CERTIFICATE OF FACSIMILE TRANSMISSION

DATE: August 21, 2006

I HEREBY CERTIFY THAT THIS PAPER IS BEING FACSIMILE TRANSMITTED TO THE PATENT AND TRADEMARK OFFICE TO FACSIMILE NUMBER 571-273-9900 ON THE DATE LISTED ABOVE.

Wendy A. Choi REG. NO. 36,697

Attention: Mail Stop "*Ex Parte* Reexam"
Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

RESPONSE PURSUANT TO 37 C.F.R. § 1.550(b)

In response to the Official Action in *Ex Parte* Reexamination dated **June 20, 2006,** reconsideration is respectfully requested in view of the amendments and/or remarks as indicated below:

- ☐ **Amendments to the Specification** begin on page of this paper.
- ☐ **Amendments to the Claims** are reflected in the listing of the claims that begins on page of this paper.
- ☐ **Amendments to the Drawings** begin on page of this paper and include an attached replacement sheet.
- ☒ **Remarks** begin on page 2 of this paper.

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REMARKS

Status of Claims

Claims 2 to 23 are subject to *ex parte* reexamination of US-B-6,919,092 ("the 092 Patent"). Claims 2 to 23 are pending. Claim 1 was previously cancelled. Claims 2, 3, 16, and 19 were previously amended. Claims 2 to 23 stand finally rejected. Patentee requests reconsideration of the rejections of claims 2 to 23.

Automatic Extension of Time

Patentee notes in accordance with M.P.E.P. § 2272 that this timely filed first response to the final rejection will automatically result in an extension of the shortened statutory period for an additional month (*i.e.*, through September 20, 2006).

Rejections

The following table summarizes the rejections maintained in the Second Office Action:

Claim	Rejection under 35 U.S.C.	Reference
3-23	§102(b)/§103(a)	Baichwal in view of Lukkari Cystrin insert
3-5, 8-10, 13-14, 16, 18-20, 23	§102(a)	Rantala
2	§102(a)	Baichwal
2	§102(e)	Baichwal
2	§103(a)	US-A-5,082,668 (Wong) PDR Robinson
2	§103(a)	US-A-5,330,766 (Morella) Robinson[1]

[1]Patentee notes that the Office maintained the rejection of claim 2 for alleged obviousness in view of the Morella patent, rather than for alleged anticipation, notwithstanding the oxybutynin-containing dosage form based on the patent that Mylan made in connection with the litigation involving US-B-6,124,355.

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All other rejections have been withdrawn. Patentee maintains its traversal of the remaining rejections, as explained more fully below, and request reconsideration of the claims in light of the amendments previously presented and following remarks.

Novelty Rejections over Rantala

Claims 3-5, 8-10, 13-14, 16, 18-20, and 23

Claims 3-5, 8-10, 13-14, 16, 18-20, and 23 stand rejected under 35 U.S.C. § 102(a) as allegedly anticipated by Example 3 and Table 4 of the Rantala application. Patentee maintains its traversal of the rejection because Example 3 does not disclose a maximum plasma oxybutynin concentration within the claimed range of about 0.28 ng/ml to about 0.45 ng/ml per mg. The Office notes that Example 3 refers to a C_{max} that it presumably divides by 10 mg to reach 0.213 ng/ml/mg. Although the Office concludes that 0.213 ng/ml/mg is "about" 0.28 ng/ml/mg oxybutynin (the lower limit recited in claim 3), the Office fails to identify any evidence supporting its apparent conclusion that those skilled in the art would deem 0.213 ng/ml/mg to be "about 0.28 ng/ml/mg" in spite of the fact that they differ by nearly 24% (*i.e.*, (0.28 – 0.213) ÷ 0.28). Accordingly, the rejection lacks evidentiary basis and should be withdrawn.

Novelty Rejections over Baichwal

Claim 2

Claim 2 stands rejected under 35 U.S.C. §§ 102(a) and (e) as allegedly anticipated by the tablet formulation of Example 3 of the Baichwal patent. Patentee maintains its traversal of the rejection because the Office has not demonstrated that this tablet formulation exhibits a zero order release rate for about 24 hours.

Contrary to the Office's position, plotting the release of drug that the Baichwal patent provides for Example 3 in Table 3 as a function of time does not produce a linear plot, much less a plot reflecting the claimed zero order release rate for about 24 hours. Although the Baichwal patent discloses controlled release delivery of oxybutynin generally, it does not

disclose linear release for about 24 hours. Furthermore, Baichwal's experimental examples appear to release the vast majority of oxybutynin in 12 hours or less; there is no disclosure in the patent of linear, or zero-order, release for about 24 hours. That Example 3 of Baichwal may occasionally produce results that fall within claim 2 would be insufficient to establish anticipation.[2] *MEHL/Biophile Intern. Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999). Accordingly, the rejection for alleged anticipation is improper and should be withdrawn.

Claim 3-23

Claim 3-23 are rejected as allegedly anticipated by Example 3 of the Baichwal patent under 35 U.S.C. § 102(b), or alternatively, as obvious under 35 U.S.C. § 103(a). Patentee maintains its traversal of these rejections because the patent does not disclose the claimed maximum plasma oxybutynin concentration of about 0.28 ng/ml to about 0.45 ng/ml per mg.

As a first consideration, the Baichwal patent does not disclose that the oxybutynin tablets of Example 3 were actually administered to any patients in the prior art, much less that such administration produced the claimed range of maximum plasma oxybutynin concentrations. The Office appears to be aware of this deficiency, because it refers to two other references that are not prior art with respect to the instant claims (*i.e.*, the product insert for the Cystrin CR product and the Lukkari reference) in an attempt to demonstrate that Example 3 of the Baichwal patent constitutes an inherent anticipation of the instant claims. These references, however, fail to demonstrate any inherency because they discuss the concept of oxybutynin plasma concentration only in the context of specific test conditions that the Baichwal patent fails to so much as mention. As even the Office recognizes, the testing that is said to be disclosed in the Lukkari reference involved administration of the dosage form under fasting conditions, one hour before breakfast, or two hours after breakfast (First Office Action at page 9). Since the Baichwal patent does not even mention administering the dosage form disclosed in Example 3 under such conditions or any conditions, there is no basis for the Office's allegations of anticipation. *Continental Can Co.*

[2]See Cystrin Stipulation. *Alza Corp. v. Mylan Labs. Inc.*, Post-Trial Memorandum Opinion and Order, page 38 (Reference 264 on Form 1449 submitted on October 21, 2005).

v. Monsanto Co., 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) (to establish inherent anticipation, extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference"). Furthermore, even if administering the Baichwal dosage form will occasionally, but not invariably, result in the claimed maximum plasma oxybutynin concentration under certain conditions, then it is not sufficient to establish anticipation. *Glaxo Inc v. Novopharm Ltd.*, 52 F.3d 1043 (Fed. Cir. 1995) (prior art that falls within the patent claims even frequently, but not invariably, is not an inherent anticipation); *MEHL/Biophile Intern. Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999) ("occasional results are not inherent").

Accordingly, the rejection for alleged inherent anticipation or, alternatively, for alleged inherent obviousness is improper and should be withdrawn.

Obviousness Rejections under 35 U.S.C. § 103(a)

Wong in combination with PDR and Robinson

Claim 2 stands rejected under 35 U.S.C. § 103(a), as allegedly obvious over the Wong patent in combination with the PDR and Robinson references. Patentee maintains its traversal of the rejection because those of ordinary skill in the art would not have been motivated to combine the respective teachings of these references, or to prepare a dosage form that releases oxybutynin at a controlled and sustained, substantially zero order release rate for about 24 hours.

That motivation for the proposed combination would have been lacking is apparent from the Office's characterization of the cited references. Indeed, the respective teachings of the Robinson reference and Wong patent that the Office alleges to be relevant are plainly inconsistent. According to the Office, for example, the Robinson reference is relevant for its disclosure that oxybutynin possesses undesirable anticholinergic side effects that can be ***reduced*** through use of a modified release formulation of the drug (First Office Action at page 15; Second Office Action at page 15). The Wong patent, by contrast, is said to be relevant for its disclosure of a dosage form for drugs that are ***intended*** to act upon cholinergic receptors (First Office Action at page 15; Second Office Action at page 16). The Office does

not reconcile this inconsistency. In fact, there is simply no reason to believe that those of ordinary skill having knowledge a drug's undesirable side effects would have been motivated to incorporate the drug into a dosage form that they understood to have been designed to achieve that side effect.

Yet another reason for withdrawal of the rejection is that the conventional wisdom prior to the claimed inventions was that orally ingested, controlled-release products had to release drug in 8 to 12 hours, before the product reached the colon, because absorption through the colon was thought to be poor and variable (See, for example, Gupta and Robinson, *Treatise on Controlled Drug Delivery: Fundamentals, Optimization, Applications*, Marcel Dekker, Inc. 1992, 255-313, 268, copy enclosed). Thus, contrary to the Office's assertions, those of ordinary skill would not have been motivated to administer oxybutynin, as claimed, over a period of about 24 hours for the purpose of treating incontinence in a patient.

Based on the foregoing reasons, the rejection for alleged obviousness is thus improper, and should be withdrawn.

Morella in view of Robinson

Claim 2 stands rejected under 35 U.S.C. § 103(a), as allegedly obvious over the Morella patent in view of the Robinson reference. Patentee maintains its traversal of the rejection because there is no motivation to combine the references, but even if there were, the combination of the respective teachings of these references would not have produced any claimed invention.

First, there is no motivation to produce an oral dosage form of oxybutynin for treating incontinence in a patient that releases over about 24 hours because the skilled artisan would not have sought to deliver the drug via colonic absorption. As discussed above with respect to Wong, the conventional wisdom prior to the claimed inventions was that orally ingested, controlled-release products had to release drug in 8 to 12 hours, before the product reached the colon, because absorption through the colon was thought to be poor and variable (*Id.* at

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268). Thus, contrary to the Office's assertions, those of ordinary skill would not have been motivated to administer oxybutynin, as claimed, over a period of about 24 hours.

Furthermore, neither the Morella patent nor Robinson reference discloses or suggests the claimed zero order release rate. Although the Office refers to Figure 5 of the Morella patent, the data points provided in the figure do not show a substantially zero order rate of release for about 24 hours. Notably, no data points are shown between 600 minutes (10 hours) and 1440 minutes (24 hours).

Thus, even if it would have been obvious to combine the respective teachings of the Morella patent and the Robinson reference (and Patentee does not concede that doing so would have been obvious), none of the resulting methods or dosage forms would have exhibited the claimed zero order release rate. Accordingly, the rejection under 35 U.S.C. § 103(a) is improper and should be withdrawn. *In re Payne*, 203 U.S.P.Q. 245, 255 (C.C.P.A. 1979) (references relied upon to support rejection under § 103 must place the claimed invention in the possession of the public).

Conclusions

Patentee respectfully requests reconsideration and withdrawal of the novelty and obviousness rejections in view of the previous amendments and foregoing remarks.

If the Examiner has any questions, the Examiner is invited to call the undersigned at (215) 568-3100.

Date: **August 21, 2006**

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